

- (1) an extracellular ligand association domain;
- (2) a spacer domain;
- (3) a transmembrane domain; and
- (4) one or more intracellular domains; provided that at least two of said domains in one chain are not naturally fused to each other, and wherein the spacer and/or transmembrane domains are selected to remain unassociated except in the presence of bound ligand.

20. A chimeric receptor according to Claim 19 wherein each extracellular ligand association domain is an antibody variable region (V_H or V_L) domain, a T-cell receptor variable region domain ($TCR\alpha$, $TCR\beta$, $TCR\gamma$, $TCR\delta$), $CD8\alpha$, $CD8\beta$, $CD11a$, $CD11b$, $CD11c$, $CD18$, $CD29$, $CD49a$, $CD49b$, $CD49c$, $CD49d$, $CD49e$, $CD49f$, $CD61$, $CD41$ or $CD51$ chain or a fragment thereof.

21. A chimeric receptor according to Claim 20 wherein each association domain is structurally different to each other.

22. A chimeric receptor according to Claim 19 wherein the ligand association domains of the chimeric receptor are a V_H domain paired with a V_L domain, two or more $TCR\alpha$, $TCR\beta$, $TCF\gamma$, and/or $TCR\delta$ domains, a $CD8\alpha$ or β homo- or heterodimer, $CD18$ paired with one or more of $CD11a$, b , or c , $CD29$ paired with one or more of $CD49a$, b , c , d , e , or f , and $CD61$ paired with $CD41c$ and/or $CD51$.

23. A chimeric receptor according to Claim 19 wherein each intracellular domain is a naturally occurring polypeptide signaling sequence.

24. A chimeric receptor according to Claim 23 wherein each signaling sequence is all or part of the zeta, eta or epsilon chain derived from the T-cell receptor; CD28; CD4; CD8; the γ chain of an Fc receptor; a signaling component from a cytokine receptor, a colony stimulating factor receptor, a tyrosine kinase and binding domains thereof; or an adhesion molecule.

25. A chimeric receptor according to Claim 19 wherein the transmembrane domain is an oligo- or polypeptide derived from all or part of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD8, CD4, CD3 ϵ , CD45 and members of the tetraspan family, a cytokine receptor, or a colony stimulating factor receptor.

26. A chimeric receptor according to Claim 19 wherein each spacer domain is a polypeptide comprising 20 to 100 amino acids.

C
27. A chimeric receptor according to Claim 19 wherein each independent polypeptide chain has a secretion signal sequence attached to the N-terminus of the association domain of each chain.

28. A chimeric receptor according to Claim 19 wherein the chimeric receptor has two independent polypeptide chains.

29. A chimeric receptor according to Claim 28 wherein one polypeptide chain has a ligand association domain which is a V_H domain or a fragment thereof, and the other has a ligand association domain which is a V_L domain or a fragment thereof.

30. A chimeric receptor of Claim 19, wherein the spacer domain is modified to remain unassociated except in the presence of bound ligand.

31. A chimeric receptor of Claim 19, wherein the transmembrane domain is modified to remain unassociated except in the presence of bound ligand.
32. A chimeric receptor of Claim 19, wherein the spacer domain is a CD8 domain.
33. A chimeric receptor of Claim 32, wherein the CD8 spacer domain is a modified CD8 spacer domain.
34. A nucleic acid sequence encoding a chimeric receptor of Claim 19 or an independent polypeptide chain thereof.
35. A nucleic acid sequence according to Claim 34 in association with a carrier.
- C 36. A nucleic acid sequence according to Claim 35 wherein the carrier is a viral vector, a liposomal vector, a cationic lipid or an antibody.
37. A nucleic acid sequence according to Claim 35 wherein the carrier is a targeted carrier.
38. A nucleic acid sequence according to Claim 34 wherein the nucleic acid sequence is on a plasmid.
39. Plasmid pHMF374 of Figure 3.
40. An effector cell containing a nucleic acid sequence or a plasmid according to Claim 34.
41. An effector cell expressing a chimeric receptor of Claim 19.